PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
Case 21372		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP 03/09112	18.08.2003	23.08.2002
International Patent Classification (IPC) or both national classification and IPC		
A23L1/302		
Applicant		
ROCHE VITAMINS AG et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
18.02.2004	02.08.2004
Name and mailing address of the international preliminary examining authority:	Authorized Officer
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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/09112

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-22 as originally filed

Claims, Numbers

1-27 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 26-27 (IA only)

because:

☒ the said international application, or the said claims Nos. 26-27 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	3-4, 7-8
	No:	Claims	1,2,5,6,9,10,13-16,18-27
Inventive step (IS)	Yes:	Claims	3-4, 7-8
	No:	Claims	1-2, 5-6, 9-27
Industrial applicability (IA)	Yes:	Claims	1-25
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 26-27 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT). However, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item V

Reasoned statement under Art. 35 (2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

V.1 Reference is made to the following documents:

D1: WO 03 028747 A (MARTIN ROBERT ;HARRIS DENNIS H (US); GENERAL RONALD E (US)) 10 April 2003 (2003-04-10)

D2: WO 02 076436 A (MEIJER JAAP) 3 October 2002 (2002-10-03)

D3: US-B1-6 203 819 (FINE STUART A) 20 March 2001 (2001-03-20)

D4: US-A-6 103 756 (GORSEK WAYNE F) 15 August 2000 (2000-08-15)

D5: WO 02 47493 A (AVENTIS PHARMA GMBH) 20 June 2002 (2002-06-20)

D6: US-A-5 976 568 (RILEY PATRICIA A) 2 November 1999 (1999-11-02)

D7: US-B1-6 291 533 (FLEISCHNER ALBERT M) 18 September 2001 (2001-09-18)

D8: US-A-5 922 704 (BLAND JEFFREY) 13 July 1999 (1999-07-13)

D9: MCCARTY M F: 'TOWARD PRACTICAL PREVENTION OF TYPE 2 DIABETES' MEDICAL HYPOTHESES, EDEN PRESS, PENRITH, US, vol. 54, no. 5, May 2000 (2000-05), pages 786-793, XP001019681 ISSN: 0306-9877

D10: EP-A-1 177 789 (ROCHE VITAMINS AG) 6 February 2002

D11: DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1999 MCCARTY MF: 'High-dose biotin, an inducer of glucokinase expression, may synergize with chromium picolinate to enable a

definitive nutritional therapy for type-II diabetes'. Database accession no.

PREV199900343017 XP002262310

V.2 **Novelty (Art. 33 (2) PCT) and inventive step (Art. 33 (3) PCT)**

V.2.1 Documents D3-D5 disclose nutritional supplements which comprise biotin and lipoic acid, for use in the treatment of diabetes or of its complications. Document D6-D8 disclose compositions comprising biotin as well as green tea and lipoic acid for use in the treatment or prevention of diabetes and syndrome X (D6), or for unrelated uses (D7, D8). The compositions of D7 additionally comprise epigallocatechin gallate. Even though these documents did not recognize the presence of synergies between biotin on one hand, and phytanic acid, or epigallocatechin gallate (EGCG), or cysteamine/pantethine on the other hand, they remain relevant for novelty (D3-D8) and inventive step (D3-D6). Other aspects to take into account are that:
- restricting a claim to foods or beverages for the delivery of the claimed combination of actives may provide novelty, but not inventive step,
- dosages expressed as mg/kg body weight do not allow to clearly distinguish the claimed compositions from those of the prior art,
- the Demand does not reveal any synergy between biotin on one hand, and policosanol, or lipoic acid, on the other hand. Thus, the presence of these compounds in the claimed compositions should be considered obvious options for a man skilled in the art, especially since their potential beneficial effects in diabetes appear well documented in the prior art.

As a result, only claims 3, 4, and 7, 8 can be considered to meet the requirements of Art. 33 (2) and (3) PCT for novelty and inventive step, as such compositions are new and provide unexpected advantages as shown by the experimental data presented on Tables 1 and 2 of the Demand.

V.2.2 Attention is drawn (R. 64.3 PCT) to documents D1 and D2, which are not comprised in the state of the art according to R. 64.1 PCT, but which might become relevant in later, regional phases. Document D1 discloses compositions comprising biotin and lipoic acid for the treatment of certain conditions occurring during diabetes. That document might become relevant in terms of novelty for claims 1, 2, 9, 10, 13-15, 21-22 and 26-27. Document D2 disclose compositions comprising biotin and lipoic acid also, however not for the treatment of diabetes. That document might therefore become relevant for the novelty of claims 1, 2, 9, 10, 13-14 and 19-23.

V.2.3 Detailed information as regard the relevant passages of the cited documents, as well as to the claims concerned with these documents, may be found in the International Search report.

V.3 The subject-matter of claims 1-25 is industrially applicable in the sense of Art. 33 (3) PCT.